

CATGAAGGTTCTCTCTGCTTCTCTTTCTTCTGTCTCAGTGCGAGCTACTGAGCAACCGCAGGTCTG
TCACTGAGCATCCAGCATGGAGGCAGCCCTGACCGGGGCCAACGCTCCTCGCACTTCTGGGGCCAACTAC
ACTTTCTCTGACTGGCAGAACTTCGTGGGCAGGAGACGTTATGGGGCCGAGTCCCAGAACCCACGGTGAA
AGCACTGCTCATCGTGGCCTACTCATTCAACATCGTCTTCTCGCTCTTCGGTAATGTCTGGTCTGTCTATG
TCATCTTCAAGAACCAGCGCATGCACTCGGCCACCAGCCTCTTCATGTCAACCTGGCAGTGGCGGACATC
ATGATCACATGCTCAACACGCCCCCTTCACTTTGGTCCGCTTTGTGAACAGCACATGGGTGTTTGGGAAGGG
CATGTGTCATGTCAGTGGCTTTGCTCAGTACTGTTCTCTACATGTCTCAGCACTGACTCTGACAGCTATCG
CAGTGGACCGCCACCAGGTCAATCATGCATCCACTGAAGCCTCGGATCTCCATCACCAAGGGTGTCTATAT
ATTGCTGTCTCTGGGTCTATGGCTACCTTCTTCTCTCTGCCACATGCCATCTGCCAGAACTGTTTACCTT
CAAGTACAGTGAGGACATTGTGGCTCCCTCTGCCCTGCCGGACTTCCCGGAGCCAGCTGACCTCTTCTGGA
AGTATCTGGACCTGGCCACCTTCATCCTGCTCTACCTACTTCCACTCTTCATTATCTCAGTGGCCTATGCT
CGTGTGGCCAAAGAAGCTGTGGCTCTGTAAACACCATTTGGCGACGTGACCACAGAGCAGTACCTCGCCCTGGC
ACGCAAGAAGAAGACCACCGTGAAGATGCTGGTGTCTGTGGTAGTCTCTTTGCCCTCTGCTGGTTCCCTC
TCAACTGCTATGTCTCTCTCTTGTCCAGCAAGGCCATCCACACCAACAATGCCCTCTACTTTGCCCTCCAC
TGGTTTGGCATGAGCAGTACTTGTATAACCCCTTCACTACTGCTGGCTCAATGAGAACTTTAGGGTTGA
GCTTAAGGCATTGCTGAGCATGTGCCAAAGGCCACCCAAAGCCGAGGAAGACAGGCTACCTTCCCGGATTTC
CTTCCTTCAGGGTGGCATGGACAGAGAAGAGCCATGGTCCGAGGGCTCCACTACC'TAATCACCACCTTGCCC
TCTTCCAGATCCAGTCTGGGAAGACAGATCTGTCTCTGTGGAACCCGTGTGGCCATGAGTTAGGGAAA
GCTGGAAGTTGGTGGGGGAGGGTTCTTTCTCTCTACAATTGACCAGACACTAACAGAGTTGGAAAGTAACA
CAGAAGCAGTGAGATGCTTGGGTTTCTAGGAACCTGTCCAGCCCCATCTGATT'TGCAAACTTTCTAGAAGA
TGCCATGAGGTGGTGTGTGTAGATCTTTGAGCAAGAGCTCTGGAAACCACCTCAGCTTCAACAGAGGCTGG
TCCAGTCAACCACCTCCAATTGTGTAGCATCTGCCACCTTGCCCTTCTACTGCTGAGCAACCACAGGGGG
ACTTGAGCCATACTATTGGTGGGCCTGCCCCACATGCTCAGAAAAGAACAGGCACAAAGGCTTTCTGAAGT
CATTGGAAACAGGAATAATCACACAGCTTCAGTGACCTTGCTCTATCCATGACCAGACAGGACCCATTTTG
GCTTCTTAAAAACAAAGAGAAATTAGTATTGCCACTTTGAAAAGTTCAGAAAAGTAAAGAAATGAGTTCAG
CCCTCAATTTGTAAAAAAGGAAAAAAGAAAAAAGAAAAAAGAAAAAGCCCTGTTAATATGCTG
TAAATTTATCTGTAGCTTTGCCCTTCTGTGTGTGTACATTTGTACTTTTAAATCCTGAACCTACAGTGTCC
ATGTAGATTGTAATAATTAGCAAGAACTGGAATATATCAGAGTAT'TATTGAATTC (SEQ ID NO:1)

MKVPPVLLLFLLSSVRATEQPQVVTEHPSMEAALTGPNASSHFWANYTFSDWQNFVGRRRYGAESQNPTVK
ALLIVAYSFTIVFSLFQNVLVCHVIFKNQRMHSATSLFIVNLAVADIMITLLNTPFTLVRFVNSTWVFGKG
MCHVSRFAQYCSLHVSALTLTAIAVDHRQVIMHPLKPRISITKGVIIYIAVIWVMATFFSLPHAICQKLFTF
KYSIEDIVRSLCLPDFPEPADLFWKYLDLATFILLYLLPLFIIISVAYARVAKKLWLCNTIGDVTTEQYLALR
RKKKTTVKMLVLVVVLFALCWFLNLCYVLLLSSKAIHTNNALYFAFHWFAMSSTCYNPFIYCWLNENFRVE
LKALLSMCQRPPKPQEDRLSPVPSFRVAWTEKSHGRAPLPNHHLPSQIQSGKTDLSSVEPVVAMS
(SEQ ID NO:2)

Figure 1

Underlined = deleted in targeting construct

Bold = sequence flanking Neo insert in targeting construct

GGGGTGGCAGTCGGCACCATCAGGCTCCCTTGGCGTTTCGGAGTTTTCTCTGTGGTCCCG
ACTCTCCGGAGGATCTCGGTTGTCTCCCAAGTCGGAACCTGGCAGGTCAGGTTCACTC
GGAGGTCCGGGCTTCTCTGTGCCCCGTGCCCTCGCTCCAGGCTCCCTCTGTGGTGTG
GACTCCTCTAGCCCCGGTGCCTCAGCCCCCTCGCACCCAGCCTCCAGGCACAGAGCCCCGC
AGGGAGCTCAGCCCTTGTGCCTAGAGCTGCAGTGGCTGGACATGAAGGTTCCCTCTGTCC
TGCTTCTCTTTCTTCTGTCTCAGTGCAGCTACTGAGCAACCGCAGGTCGTCACTGAGC
ATCCCAGCATGGAGGCAGCCCTGACCGGGCCCAACGCCTCCTCGCACTTCTGGGCCAACT
ACACTTTCTCTGACTGGCAGAACTTCGTGGGCAGGAGACGTTATGGGGCCGAGTCCCAGA
ACCCACGGTGAAAGCACTGCTCATCGTGGCTACTCATTACCATCGTCTTCTCGCTCT
TCGGTAATGTCTGGTCTGTCTATGTCTTCAAGAACCAGCGCATGCACCTCGGCCACCA
GCCTCTTCAATTGTCAACCTGGCAGTGGCGGACATCATGATCACATTGCTCAACACGCCCT
TCACTTTGGTCCGCTTGTGAACAGCACATGGGTGTTTGGGAAGGGCATGTGTCTATGTCA
GTCGCTTTGCTCAGTACTGTCTCTACATGTCT**CAGCACTGACTCTGACAGCTATCGCAG**
TGGACCGCCACCAGGTCACTCATGCATCCACTGAAGCCTCGGATCTCCATCACCAAGGGTG
TCATATATATTGCTGTCTATCTGGGTCTATGGCTACCTTCTTCTCTCTGCCACATGCCATCT
GCCAGAACTGTTTACCTTCAAGTACAGTGAAGACATTTGTGCGCTCCCTCTGCCTGCCGG
ACTTCCCGGAGCCAGCTGACCTCTTCTGGAAGTATCTGGACCTGGCCACCTTCATCCTGC
TCTACCTACTTCCACTCTTCATTATCTCAGTGGCTATGCTCGTGTGGCCAAAGAAGCTGT
GGCTCTGTAACACCATTGGCGACGTGACCACAGAGCAGTACCTCGCCCTGCGACGCAAGA
AGAAGACCACCGTGAAGATGCTGGTGTCTTGTGGTAGTCTCTTTGCCCTCTGCTGGTTCC
CTCTCAACTGCTATGTCTCTCTCTTGTCCAGCAAGGCCATCCACACCAACAATGCCCTCT
ACTTTGCCTTCCACTGGTTTGCCATGAGCAGTACTTGTATATAACCCCTTCATCTACTGCT
GGCTCAATGAGAACTTTAGGGTTGAGCTTAAGGCATTGCTGAGCATGTGCCAAAGGCCAC
CCAAGCCGCAGGAAGACAGGCTACCTTCCCCAGTTCCCTCCCTCAGGGTGGCATGGACAG
AGAAGAGCCATGGTGGAGGGCTCCACTACCTAATCACCACTTGGCCCTCTTCCCAGATCC
AGTCTGGGAAGACAGATCTGTCTATCTGTGGAACCCGTGTGGCCATGAGTTAGGGAAAGC
TGGAAAGTTGGTGGGGGAGGGTTCTTTCTCTCTACAATTGACCAGACACTAACAGAGTTGG
AAAGTAACACAGAAGCAGTGAAGTGTCTGGGTTCCCTAGGAACCTGTCCAGCCCCATCTGA
TTTGCAAACTTTCTAGAAGATGCCATGAGGTGGTGTGTGTAGATCTTTGAGCAAGAGCTC
TGGAAACCACCTCAGCTTCAACAGAGGCTGGTCCAGTCAACCACCTCCAATTGTGTAGCA
TCTGCCACCTTGCCCTTCTCTACTGCTGAGCAACCACAGGGGGACTTGAGCCATACCTATTG
GTGGGCCCTGCCCCACATGCTCAGAAAAGAAGGCACAAAGGCTTTCTGAAGTCATTGGA
ACAGGAATAATCACACAGCTTCAGTGAACCTTGGCTCTATCCATGACCAGACAGGACCCAT
TTTGGCTTCTTAAAAACAAAGAGAAATTAGTATTGCCACTTTGAAAAGTTCAGAAAAGTA
AAGAAATGAGTTTCAGCCCTCAATTTGTAAAAAAGGAAAAAAGAAAAAAGAAAAAAG
AAAGAAAAAAGCCTGTAAATATGCTGTAAATTTATCTGTAGCTTTGCCTTCTGTGTGTGT
ACATTTGTACTTTTAAATCCTGAACTACACGTGTCCATGTAGATTGTAATAATTAGCAA
GAAACTGGAATATATCAGAGTATTATTGAATTC

Figure 2A

Gene Sequence
Structure *

299 bp

Sequence Deleted

753 bp

Size of partial
cDNA: 2253 bp

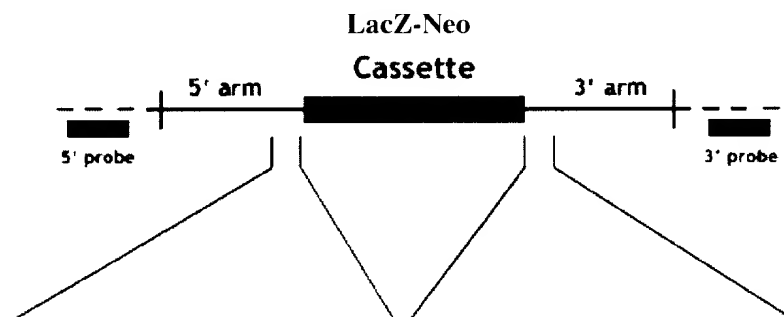
Targeting Vector* (genomic sequence)

Construct Number: 463

Arm Length:

5': 2.5 kb

3': 0.6 kb



———— Targeting Vector
- - - - Endogenous Locus

* Not drawn to scale

5' >CTGGCACGGTCCAGGTTCACT
CGGAGGCCCGGGCTTCCTCTGTGC
CCCGTGCCCTCGCTCCCTGGCTC
CCTCTGTGGTGTGGACTCCTCTAG
CCCGGTGCGCTCAGCCCTCGCAC
CCAGCCTCCAGGCACAGAGCCCGG
CAGGGAGCTCAGCCCTTGTGCCTA
GAGCTGCAGTGGCTGGACATGAAG
GTTTCTCCTGT<3'
(SEQ ID NO:3)

5' >CAGCACTGACTCTGACAGCTA
TCGCAGTGGACCGCCACCAGGTGA
GAGCACCTGTCCCCAGCAGCATGC
TCCCATCTCCGTCTATGCCTGGCT
GGCTGGTGGGAATACTGCCACCAC
GGTCTGTAGGGAATACTCTCAGGA
CAGTGACTCATTTCAGTCCCGCTGA
CAGCGTGTGTGCTTGCCTCCTTGT
TGATCAATTTG<3'
(SEQ ID NO:4)

Figure 2B